CLAIMS

ANALOGUES OF LIPOPOLYSACCHARIDE-BINDING PROTEIN (LBP)-DERIVED PEPTIDES THAT EFFICIENTLY NEUTRALIZE LIPOPOLYSACCHARIDES (LPS).

1. An LPS-binding and –neutralizing peptide comprising the amino acid sequence X-1-2-3-4-5-6-7-8-9-10-11-12-13-14-Y, wherein:

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X is a linear chain from zero to four amino acids.

(1) is one of the amino acids alanine, threonine, glutamine, asparagine or serine; and if and only if at least one of the a.a. at positions +5, +9, +10, +11 or +13 has been replaced (from the native LBP sequence) according to what is herein described, then (1) could also be arginine or lysine.

(2) is one of the amino acids alanine, valine, isoleucine, leucine, phenylalanine, methionine, tryptophan or tyrosine.

(3) is one of the amino acids glutamine, asparagine, serine or threonine.

(4) is one of the amino acids glycine, alanine, valine, isoleucine, leucine, phenylalanine, methionine, tryptophan or tyrosine.

(5) is one of the amino acids alanine, threonine, glutamine, asparagine or serine; and if and only if at least one of the a.a. at positions +1, +9, +10, +11 or +13 has been replaced according to what is herein described, then (5) could also be arginine or lysine.

(6) is one of the amino acids tryptophan or phenylalanine.

(7) is one of the amino acids lysine or arginine.

(8) is one of the amino acids alanine, valine, isoleucine, leucine, phenylalanine or tyrosine.

(9) is one of the amino acids alanine, threonine, glutamine, asparagine or serine; and if and only if at least one of the a.a. at positions +1, +5, +10, +11 or +13 has been replac d according to what is herein described, then (9) could also be arginine or lysine.

(10) is one of the amino acids alanin , valine, isoleucine, l ucine, phenylalanine, methionine, tryptophan or tyrosine; and if and only if at l ast one of the a.a. at positions +1, +5, +9, +11 ó +13 has been replaced according to what is herein described, then (10) could also be lysine or arginine.

(11) is one of the amino acids alanine or valine; and if and only if at least one of the a.a. at positions +1, +5, +9, +10, o +13 has been replaced according to what is herein described, then (11) could also be serine; and if and only if the a.a. at position +10 has been replaced according to what is herein described, then (11) could also be threonine, glutamine, asparagine, lysine or arginine.

(12) is one of the amino acids phenylalanine, tryptophan or tyrosine.

(13) is one of the amino acids alanine, threonine, glutamine, asparagine or serine; and if and only if at least one of the a.a. at positions +1, +5, +9, +10 ó +11 has been replaced according to what is herein described, then (13) could also be phenylalanine, arginine or lysine; and if and only if the a.a at position +14 is lysine or arginine, then (13) could also be glycine.

(14) is one of the amino acids lysine, arginine or alanine, and if and only if the a.a. at position +13 has been replaced according to what is herein described, then (14) could also be valine , isoleucine, leucine, phenylalanine, methionine, tryptophan or tyrosine.

Y is a linear chain from zero to four amino acids.

2. A peptide according to claim 1 having the ability to bind and neutralize LPS which is the N-terminal region of a larger polypeptide.

3. A peptide according to claim 1 having the ability to bind and neutralize LPS which is the C-terminal region of a larger polypeptide.

4. A peptide according to claim 1 having the ability to bind and neutralize LPS which is inserted into the linear chain of a larger polypeptide.

5. A peptide according to claim 1 wherein at least one amino acid of said sequence has been substituted by a non-natural homologous amino acid.

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6. A peptide according to claim 1 wherein the N-terminus has be n modify by acetylation or succinylation.

7. A polypeptide according to claim 2 wherein the N-terminus has been modify by acetylation or succinylation.

8. A peptide according to anyone of claims 1 or 3 wherein the C-terminus is a -OH, -COOH or $-CONH_2$ group.

9. A peptide according to claim 1 that has been constrained to adopt a cyclic conformation by an intramolecular disulfide or amide bond.

10. A peptide according to claim 5 that has been constrained to adopt a cyclic conformation by an intramolecular disulfide or amide bond.

11. A peptide according to claim 1 wherein the chain backbone have been substituted by backbone-mimetic organic entities.

12. A peptide according to anyone of claims 5, 6, 9 or 10 wherein the chain backbone have been substituted by backbone-mimetic organic entities.

13. A peptide according to anyone of claims 1, 5, 6, 9 or 10 wherein at least one amino acid of said sequences have been substituted by alkylation using chemical or enzymatic methods.

14. A peptide according to anyone of claims 1, 5, 6, 9 or 10 wherein at least one amino acid of the said sequences have been glycosylated using chemical or enzymatic methods.

15. A linear polypeptide chain containing two or more repeats of a peptide sequence according to anyone of claims 1 or 5 connected by 12-25 amino acid linkers, rich in glycine, alanine, proline or serine residues.

16. An arrangement of three of more copies of homologous peptide sequences or combinations of different sequences, according to anyone of claims 1 or 5, linked by their C-terminus to a lysine core structure.

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17. A pharmaceutical composition comprising effective amounts of a peptide according to claim 1, and a pharmaceutically acceptable diluent, carri r or adjuvant.

18. A pharmaceutical composition comprising effective amounts of a molecule according to anyone of claims 2 to 4, and a pharmaceutically acceptable diluent, carrier or adjuvant.

19. A pharmaceutical composition comprising effective amounts of a molecule according to claim 5, and a pharmaceutically acceptable diluent, carrier or adjuvant.

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20. A pharmaceutical composition comprising effective amounts of a molecule according to anyone of claims 6 to 16, and a pharmaceutically acceptable diluent, carrier or adjuvant.

21. The use of the pharmaceutical composition according to claim 17 for the treatment of Systemic Inflammatory Response Syndrome.

22. The use of the pharmaceutical composition according to claim 17 for the treatment of Gram-negative sepsis and its sequelae.

23. The use of the pharmaceutical composition according to claim 17 for the treatment of obstructive jaundice.

24. The use of the pharmaceutical composition according to claim 17 for the treatment of inflammatory bowel diseases.

25. The use of the pharmaceutical composition according to claim 17 for the treatment of bacteremia.

26. The use of the pharmaceutical composition according to claim 17 for the treatment of osteomyelitis.

27. The use of the pharmaceutical composition according to claim 17 for the treatment of patients at risk of developing sepsis.

28. The use of the pharmaceutical composition according to claim 17 for methods to treat chronic infections, arthritis or rheumatic disorders.

Add A3

add A4 on a seperate page

add C1